

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
21 October 2004 (21.10.2004)

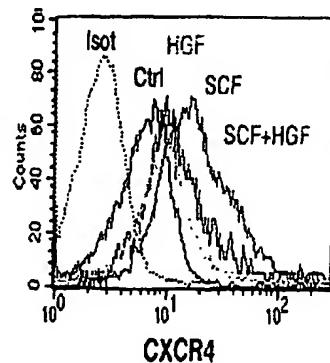
PCT

(10) International Publication Number
WO 2004/090121 A3

- (51) International Patent Classification⁷: C12N 5/06,
C07K 14/00, A61K 38/19
- (21) International Application Number:
PCT/IL2004/000315
- (22) International Filing Date: 7 April 2004 (07.04.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
155303 8 April 2003 (08.04.2003) IL
159307 10 December 2003 (10.12.2003) IL
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- (52) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (54) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),

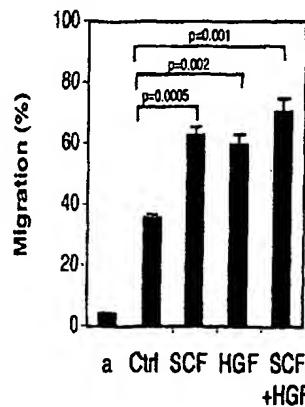
[Continued on next page]

(54) Title: STEM CELLS HAVING INCREASED SENSITIVITY TO A CHEMOATTRACTANT AND METHODS OF GENERATING AND USING SAME



A

(57) Abstract: The present invention relates to stem cells which exhibit increased sensitivity to a chemoattractant and, more particularly, to methods of generating and using them such as in clinical applications involving stem cell transplantation.



B

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Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(88) Date of publication of the international search report:
29 December 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Published:

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000315

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12N5/06 C07K14/00 A61K38/19

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 02/50263 A (IMP COLLEGE INNOVATIONS LTD; FORBES STUART (GB); THEMIS MIKE (GB); TH) 27 June 2002 (2002-06-27)</p> <p>page 3, line 10 - line 12 page 4, line 26 page 5, line 10 page 8, line 10 - line 11 page 19, line 9 - page 20, line 6 page 22, line 13 - line 22 page 32, line 8 - page 34, line 4</p> <p>-----</p> <p style="text-align: right;">-/-</p>	<p>1-3, 5, 8, 9, 11-13, 15, 18-21, 23, 26, 47, 50-52, 55, 62, 66, 69-71</p>

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
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- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

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- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search Date of mailing of the International search report

29 October 2004

15. 11. 2004

Name and mailing address of the ISA

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Nichogianopoulou, A

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000315

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 550 769 A (TORAY INDUSTRIES) 14 July 1993 (1993-07-14) page 3, line 52 - line 53; claims 1,4; examples 8,9 -----	1-7, 11-13, 15-17, 19-21, 23-25, 27-30, 32,33, 62,63, 66-68, 71-74
X	NISHINO T ET AL: "HEPATOCYTE GROWTH FACTOR AS A HEMATOPOIETIC REGULATOR" BLOOD, W.B. SAUNDERS, PHILADELPHIA, VA, US, vol. 85, no. 11, 1 June 1995 (1995-06-01), pages 3093-3100, XP000564571 ISSN: 0006-4971 page 3094, left-hand column, paragraph 2 - paragraph 3 -----	1-3,5,8, 62,63, 66,69
X	US 5 968 501 A (COMOGLIO PAOLO) 19 October 1999 (1999-10-19) column 2, line 35 - line 59; examples 3,4,6 -----	1-6, 19-21, 23-25, 27-30, 32, 62-67, 71,73,74
P,X	KOLLET ORIT ET AL: "HGF, SDF-1, and MMP-9 are involved in stress-induced human CD34+ stem cell recruitment to the liver." JOURNAL OF CLINICAL INVESTIGATION, vol. 112, no. 2, July 2003 (2003-07), pages 160-169, XP002289611 ISSN: 0021-9738 page 162, right-hand column, last paragraph; figure 5 page 166, left-hand column, line 4 - page 167, left-hand column, line 4 -----	1-6, 62-67
A	PELED AMNON ET AL: "Dependence of human stem cell engraftment and repopulation of NOD/SCID mice on CXCR4" SCIENCE (WASHINGTON D C), vol. 283, no. 5403, 5 February 1999 (1999-02-05), pages 845-848, XP002289612 ISSN: 0036-8075 page 848, left-hand column, paragraph 2; figure 4 -----	1-18, 36-46, 56-70

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000315

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/06704 A (LAPIDOT TSVEE ; PELED AMNON (IL); YEDA RES & DEV (IL)) 10 February 2000 (2000-02-10) page 4, line 27 - line 33; claim 15 -----	1-18, 36-46, 56-70

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2004/000315

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 11-18, 36-46 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-18, 36-46, 56-70

Methods of increasing the sensitivity of stem cells to a chemoattractant, relating to the use of hepatic growth factor (HGF).

2. claims: 19-35, 71-74

Methods of treating a disorder requiring cell or tissue replacement by providing HGF.

3. claims: 47-55

Stem cells and cell lines comprising nucleic acids encoding HGF.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IL2004/000315

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0250263	A	27-06-2002	AU WO	1624302 A 0250263 A2		01-07-2002 27-06-2002
EP 0550769	A	14-07-1993	AT CA DE DE EP ES WO JP US	191501 T 2092542 A1 69230879 D1 69230879 T2 0550769 A1 2143990 T3 9303061 A1 3395181 B2 6221359 B1		15-04-2000 27-01-1993 11-05-2000 03-08-2000 14-07-1993 01-06-2000 18-02-1993 07-04-2003 24-04-2001
US 5968501	A	19-10-1999	IT AT AU AU CA DE DE DK EP JP WO ES PT	1271088 B 225183 T 707259 B2 4299696 A 2205914 A1 69528473 D1 69528473 T2 793503 T3 0793503 A1 10509951 T 9615802 A1 2183890 T3 793503 T		26-05-1997 15-10-2002 08-07-1999 17-06-1996 30-05-1996 07-11-2002 10-07-2003 03-02-2003 10-09-1997 29-09-1998 30-05-1996 01-04-2003 28-02-2003
WO 0006704	A	10-02-2000	AU CA EP WO	4926899 A 2336490 A1 1100874 A2 0006704 A2		21-02-2000 10-02-2000 23-05-2001 10-02-2000